



Lutte intégrée contre les insectes vecteurs de maladies humaines et animales. Développer la lutte génétique

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> INTEGRATED MANAGEMENT OF INSECT VECTORS OF HUMAN
AND ANIMAL DISEASES

Developing genetic control

Jérémy BOUYER

The evolution of insecticide resistance in insect vectors of human and animal diseases and the introduction of exotic vectors to new territories, in a context of tighter regulations on approved molecules, call for the development of new pest control methods.

Among these new methods, genetic control shows promise, as demonstrated by the tsetse fly eradication project in Senegal. It nevertheless requires complementary studies combining public and private research. Moreover, it must be combined with other methods of pest control – chemical, physical and biological – within an integrated management framework.

Awareness of the toxicity of insecticides to living organisms and ecosystems is leading a growing number of countries to reduce the number of approved molecules. For example, in 2014, the European Union was still authorising only four classes of vector control insecticides, and only three new classes are being developed, for operational use no earlier than 2019. Moreover, resistance to pyrethroids, the most common class used against insects, is spreading, which could result in its disuse in the short-term.

These regulations are being tightened amid growing pressure from insect vectors of human and animal diseases. This pressure is explained

by greater resistance to insecticides, but also by global factors, such as climate change or growth in trade. These global factors foster the invasion of new territories by exotic vectors. For example, the midge *Culicoides imicola*, a vector of blue-tongue disease native to tropical Africa, is invading Europe from the south. This disease caused an unprecedented health crisis in the French ruminant sector between 2006 and 2008. The tiger mosquito, *Aedes albopictus*, which is native to Asia and a major vector of arboviruses in humans, caused indigenous cases of dengue and chikungunya in mainland France in 2014. Innovations are therefore urgently required in the field of vector control.

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This eradication campaign opens up economic and environmental opportunities, and an ex-ante cost-benefit analysis has demonstrated its profitability. For a total cost of 6 400 euros per km² to the government of Senegal and international donors for permanent tsetse fly eradication, after 10 to 20 years (depending on the innovation scenario), the project would generate 2 800 euros per km² per year in additional sales of animal products (milk and meat) for the community of beneficiary livestock farmers. IVEMA places integrated pest control at the core of its strategy, associating chemical, biological and mechanical methods according to the conditions for action, and optimising their association



• In Senegal, tsetse fly eradication improves cattle productivity (pedal of gyrocopter releasing sterile tsetse males over transhumant zebus between baobabs in the Niayes area in Senegal) © J. Bouyer.

• through a significant modelling element. By supporting genetic control through field research, this project has succeeded in reducing the use of insecticide treatments (in terms of their frequency or dosage) and in developing the sterile insect technique.

• The innovative elements of this project are currently being transferred to other tsetse fly eradication projects in Africa, within the framework of PATTEC (the African Union Pan African Tsetse and Trypanosomosis Eradication Campaign). Many of them will also help to improve mosquito control in other parts of the world.

• However, implementing SIT requires sufficient quantities of sterile males to overwhelm the target population, and also a number of sterile males exceeding that of wild males. To overcome these obstacles, a variant of SIT, known as “boosted SIT”, has been developed. It aims to reduce by 90 to 99% the quantity of sterile males needed to control or eradicate a target population. In this variant, sterile males are considered as a specific means of contaminating females with a control agent. This agent may be an active substance, bacteria, a fungus or a virus, or even recombinant versions of these pathogens. But this is dependent on two conditions: avoiding contamination of species other than the target species; and avoiding dissemination after the

> New cooperation strategies are needed, implying attitude changes among partners

insect’s death. Developing this kind of biocide implies a risk assessment, guaranteed by close cooperation between public research and industries.

Involving public research and industries

Collaboration between public research and private research is needed not only for the large-scale use of transgenic insects, but also for the development of new control methods and to guarantee their safety and sustainability. All partners will benefit from this.

The large-scale use of sterile insects implies mobilising extensive research and development programmes, such as the ones leading to the eradication of the screw-worm, an insect of veterinary concern, in North America, Central America and Libya, and of the Mediterranean fruit fly, of agricultural concern, in Mexico – this fly is the subject of an SIT pest control programme in Spain. However, public research cannot implement these programmes alone, but can contribute to them by conducting the operational research essential to their optimisation and their success.

As for industries, they are faced with stricter regulations limiting the number of approved molecules and with the shorter lifespan of these molecules because of resistance. It is therefore in their interest to invest in the development of new non-toxic control methods, and to deploy these within an integrated pest control framework, taking into account lessons learned from past experience. Public research can make significant contributions to both processes.

Another area of collaboration is the assessment and management of the impact of chemical molecules used and of risks associated with the use of transgenic insects. To ensure that chemical molecules can be used in the long term, their effects on vector populations, as well as the changes caused, must be evaluated. As for transgenic insects, their use is booming. Releases of *Aedes aegypti* mosquitoes (another major vector of arboviruses) that have been genetically modified to atrophy the wings of female descendants and to prevent them from flying, have succeeded in eliminating more than 90% of target populations in parts of the Cayman Islands, Panama and Brazil. Testing in natural habitats has been authorised in Malaysia, Mexico and the United States, while trials under controlled conditions

A few words about...

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is a veterinary entomologist at CIRAD. He has been in charge of the Vectors team within the CMAEE research unit (Emerging and Exotic Animal Disease Control) since 2009 (<http://umr-cmaee.cirad.fr/>) and is associated with the INTERTRYP research unit (Host-Vector-Parasite-Environment Interactions in Neglected Tropical Diseases due to Trypanosomatids). After CIRDES (Burkina Faso) from 2001 to 2008, he worked at ISRA (Senegal) from 2009 to 2015 to support the tsetse fly eradication project in the Niayes area, before being posted to Ethiopia. He received the Agence Universitaire de la Francophonie 2015 award for young researchers in the "Science and medicine" category.

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- have been authorised in four European countries including France, and an application is pending for testing in natural habitats in Spain. Moreover, in France, the Plan Santé Environnement (PNSE 3 – environmental health plan) 2015-2019 encourages the development of research on the sterile insect technique for mosquitoes. The use of transgenic insects therefore requires a case-by-case analysis of risks, since the risk depends on the genetic mechanisms used, and in particular on their potential for dissemination. In Europe, this analysis can be based on EFSA (European Food Safety Authority) recommendations.
- New collaboration strategies are therefore required, involving a change of attitude among

partners. Industries are invited to take risks and to accept the need to phase out their reliance on chemicals in favour of diversified strategies. And researchers need to open up to industries in order to turn their inventions into innovations.

Although genetic control has potential that must be exploited, no technique should be automatically ruled out, and it is essential to analyse the advantages, disadvantages and risks associated with each one. This implies gaining further knowledge of the ecology of target vector populations, but also of the socio-ecosystems concerned by vector control. It will then be possible to achieve an optimal combination of several different methods, with the help of modelling processes. <

This *Perspective* stems from the IVEMA project, financed within the framework of ANR funding for the Institut Carnot Santé Animale (ICSA) excellence network, and the tsetse fly eradication project in Senegal, coordinated by the Direction des Services Vétérinaires du Sénégal, in partnership with the Institut Sénégalais de Recherches Agricoles, the joint FAO-IAEA division on insect pest and vector control, and CIRAD. In addition, IVEMA has established partnerships with private companies: Mubarqui, a Mexican company that developed the automatic machine for the aerial release of sterile males; the pharmaceutical groups Ceva Santé Animale and Virbac; the French start-up Long Lasting Innovation (L2I); and the company Savana.

At Expo Milano 2015, the tsetse fly eradication project won second prize in the category "Best sustainable development practices in small rural communities", as an example of ecological intensification.

This research has resulted in the following publications:

Bouyer F., M. T. Seck, A. Dicko, B. Sall, M. Lo, M. Vreysen, E. Chia, J. Bouyer & A. Wane, 2014. Ex-ante cost-benefit analysis of tsetse eradication in the Niayes area of Senegal. *PloS Negl. Trop. Dis.* 8: e3112.

Bouyer J. & T. Lefrançois, 2014. Boosting the sterile insect technique to control mosquitoes. *Trends Parasitol.* 30: 271-273.

Dicko A. H., R. Lancelot, M. T. Seck, L. Guerrini, B. Sall, M. Lo, M. J. B. Vreysen, T. Lefrançois, F. Williams, S. L. Peck & J. Bouyer, 2014. Using species distribution models to optimize vector control: the tsetse eradication campaign in Senegal. *Proceedings of the National Academy of Sciences* 111: 10149-10154.

It has also given rise to a presentation (www.isntd.org/#/isntd-bites-15-bouyer/4589861215) and an interview (www.isntd.org/#/isntd-bites-15-interv-bouyer/4589652779) that reflects the opinion of the author and not that of CIRAD, and can be found online on the website of the International Society for Neglected Tropical Diseases.



perspective

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- Alphey L., 2014. Genetic Control of Mosquitoes. *Annu. Rev. Entomol.* 59: 205 (*for a review of the potential for dissemination of different genetic mechanisms*).
- McGraw E. A. & S. L. O'Neill, 2013. Beyond insecticides: new thinking on an ancient problem. *Nat Rev Microbiol* 11: 181-193 (*for a review of credible alternatives to insecticides*).
- Suckling D. M., P. C. Tobin, D. G. McCullough & D. A. Herms. 2012. Combining tactics to exploit Allee effects for eradication of alien insect populations. *J. Econ. Entomol.* 105: 1-13 (*for a review of the integration of different pest control methods*).